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4467-102 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of Zenhausern, F.	
Serial No. 09/332,659	Group Art Unit: 1655
Filed: June 14, 1999	Examiner: Chakrabarti, A.
For: APPARATUS AND METHOD FOR MONITORING MOLECULAR SPECIES WITHIN A MEDIUM	

Do not Enter
Amdt. fr. Chakrabarti
9/30/02

Commissioner for Patents
Washington, D.C. 20231

SIR:

AMENDMENT UNDER RULE 1.116

In response to the Office Action dated March 21, 2002, please amend the application as follows:

In the Claims:

Please amend claim 1 as follows:

1. (Twice Amended) A method for monitoring an enzymatic mediated biomolecular reaction, which reaction is performed in a medium comprising at least one biomolecule, the method comprising the steps of:

screening the medium with a screening means comprising a n number of sensing probes, where n is an integer of at least one so that more than one physical, chemical, or physico-chemical change of a gas or vapor phase of at least one secondary product of the biomolecule, a biomolecule byproduct or the biomolecule which defines the information is detected by the probe to produce at least one signal output, said medium is a mixture of one or more of enzymatic products, amplicon byproducts, primer byproducts, cloned products, polymerase chain (PCR) products, secondary products, PCR byproducts or reagents and said biomolecule is at least one of DNA, RNA or a nucleotide;

transferring the signal output to a signal processing means responsive to differences in electromagnetic properties of the signal for generating a final output;

receiving the final output into a pattern recognition means sufficient to generate a measurement pattern of the information;

B1 sorting the information in accordance with a set of class boundaries of physical, chemical or physico-chemical changes of the biomolecule representative of the presence and quantitative amounts of the biomolecule in the medium; and

monitoring the sorted information for monitoring said enzymatic mediated biomolecular reaction.

Please add claims 42-44 as follows:

42. (New) A method according to claim 1, wherein the enzymatic mediated biomolecular reaction is a polymerase chain reaction.

B2 43. (New) A method according to claim 42, wherein said polymerase is selected from DNA templates and/or RNA mixtures thereof.

44. (New) A method according to claim 43 wherein said polymerase is a Taq-mediated PCR.

Please cancel claims 34, 38 and 39.

REMARKS

The Office Action dated March 21, 2002 has been carefully considered. Claims 1 and 38 have been amended. Claims 34, 38 and 39 have been cancelled. Claims 42-44 have been added. Claims 1-19, 21, 25, 26, 35-37, and 40-44 are in this application.

Claim 1 has been amended to further define the present invention. Support for claim 1 is found throughout the specification and in particular on page 11, lines 20-21; page 14, lines 9-11; page 26, line 5-page 27, line 25 and page 30, lines 12-15. Support for new claim 42 is found throughout the specification and in particular on page 12, lines 1-2. Support for new claim 43 is found throughout the specification and in particular on page 12, lines 11-13, page 13, line 25 and page 28, line 24. Support for new claim 44 is

found throughout the specification and in particular on page 34, lines 5-25. No new matter has been entered.

The previously-presented claims were rejected under 35 U.S.C. § 103 as obvious in view of Nova et al. in combination with Payne et al., Ashe et al. or Ghahramani et al. Applicant submits that the teaching of these references do not disclose or suggest the invention defined by the amended claims.

Nova et al. teach tagging molecules during synthesis of chemical compounds using matrices with memories. The matrix materials with memories can be used to tag cells for uses in cell sorting, to identify molecules in combinatorial syntheses, to label monoclonal antibodies, to tag constituent members of phage displays, affinity separation procedures, to label DNA and RNA, in nucleic acid amplification reactions.

In contrast to the invention defined by the present claims, Nova et al. do not teach or suggest a method for monitoring an enzymatic mediated biomolecular reaction by screening a biomolecule which is at least one of DNA, RNA or a nucleotide in a medium comprising a mixture of one or more of enzymatic products, amplicon byproducts, primer byproducts, cloned products, polymerase chain (PCR) products, secondary products or PCR byproducts containing at least one with a sensing probe so that more than one physical, chemical or physico-chemical change of a gas or vapor phase of the secondary product of the biomolecule, the by product of the biomolecule or the biomolecule is detected. To the contrary, Nova et al. detect a species based on fluorescence properties of linked compounds. Furthermore, the invention defined by the present claims is compatible for monitoring said enzymatic-mediated biomolecular reaction in real-time while Nova et al. does not present any detection component capable to provide such information about the reaction kinetics.

Further, Nova et al. do not teach or suggest monitoring a polymerase chain reaction, as defined by claim 42. In addition, Nova et al. do not teach or suggest that the polymerase is a DNA template, RNA template or Taq-mediated PCR. As described on page 11, lines 19-21 and page 13, lines 16-18 of the present application, the present invention has the advantage of direct monitoring of a polymerase chain reaction without fluorescent labeling. The requirement of fluorescent labeling has severe constraints such

as requiring for spectrally resolvable dyes, photobleaching and quantum efficiency (see page 26, lines 12-15). There is no teaching or suggestion in Nova et al. of monitoring a polymerase chain reaction by sensing a gas or vapor phase of the secondary product of the biomolecule, the by product of the biomolecule or the biomolecule is detected. Accordingly, the invention defined by the present claims is not obvious in view of Nova et al.

Payne et al. disclose a method for detecting a microorganism by extracting gas or vapor associated with the microorganism and flowing the same over an array of sensors. The microorganism is a bacteria typically occurring during a fermentation process. In contrast to the invention defined by the present claims, Payne et al. do not teach or suggest a method for monitoring an enzymatic mediated biomolecular reaction by screening a biomolecule which is at least one of DNA, RNA or a nucleotide in a medium comprising a mixture of one or more of enzymatic products, amplicon byproducts, primer byproducts, cloned products, polymerase chain (PCR) products, secondary products or PCR byproducts containing at least one with a sensing probe so that more than one physical, chemical or physico-chemical change of a gas or vapor phase of the secondary product of the biomolecule, the by product of the biomolecule or the biomolecule is detected. Moreover, Payne et al. do not teach or suggest monitoring a biomolecule comprising DNA, RNA or a nucleotide. Rather, Payne et al. teach methods for monitoring bacteria which are unrelated to monitoring enzymatic mediated biomolecular reactions.

Ashe et al. disclose a method for controlling the manufacture of lubricating oils involving the steps of distillation, extracting, and dewaxing for controlling operating units having feedstocks boiling above 350°C. Applicant submits that Ashe et al. teach away from the present invention by teaching a temperature range that is not compatible with the enzymatic-mediated biomolecular reaction of the present invention which reactions are typically performed in the range of 20-100°C above which temperature the enzyme would be denaturated. In contrast to the invention defined by the present claims, Ashe et al. do not teach or suggest a method for monitoring an enzymatic mediated biomolecular reaction by screening a biomolecule which is at least one of DNA, RNA or a nucleotide

in a medium comprising a mixture of one or more of enzymatic products, amplicon byproducts, primer byproducts, cloned products, polymerase chain (PCR) products, secondary products or PCR byproducts containing at least one with a sensing probe so that more than one physical, chemical or physico-chemical change of a gas or vapor phase of the secondary product of the biomolecule, the by product of the biomolecule or the biomolecule is detected. Instead, Ashe et al. is directed to an oil refining method which is unrelated to a method of monitoring enzymatic mediated biomolecular reactions or monitoring a polymerase chain reaction.

Furthermore, applicants submit that there is no motivation for one of ordinary skill in the art to combine unrelated technologies of Nova et al. directed to use of a solid matrix material with a memory for biochemical synthesis with Ashe et al. directed to a method for preparing lubricating oils. However, even if the references were combined, the combination does not teach the invention defined by the present invention since neither Nova et al. alone or in combination with Ashe et al. teach or suggest monitoring enzymatic mediated biomolecular reactions by sensing DNA, RNA or a nucleotide based on its gas or vapor phase.

Ghahramani et al. disclose a multiple hazard marker system to be combined with a deployment vehicle. The deployment vehicle can be a military tank. The sensed hazards are microorganisms, bacteria and virus. Ghahramani et al. teach monitoring a microorganism which is not related to enzymatic mediated biomolecular reactions as defined by the present claims.

Accordingly, neither Nova et al. alone or in combination with Payne et al., Ashe et al., Ghahramani et al. teach the invention defined by the present claims since none of the references teach or suggest a method for monitoring an enzymatic mediated biomolecular reaction by screening a biomolecule which is at least one of DNA, RNA or a nucleotide in a medium comprising a mixture of one or more of enzymatic products, amplicon byproducts, primer byproducts, cloned products, polymerase chain (PCR) products, secondary products or PCR byproducts containing at least one with a sensing probe so that more than one physical, chemical or physico-chemical change of a gas or vapor phase of the secondary product of the biomolecule, the by product of the biomolecule or the

biomolecule is detected. Thus, the invention defined by the present claims is not obvious in view of Nova et al. in combination with Payne et al., Ashe et al. or Ghahramani et al.

In view of the foregoing, Applicant submits that all pending claims are in condition for allowance and request that all claims be allowed. The Examiner is invited to contact the undersigned should he believe that this would expedite prosecution of this application. It is believed that no fee is required. The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 13-2165.

Respectfully submitted,

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